REMARKS

Applicants would like to thank the Examiner for withdrawing the finality of the last Office Action and reopening prosecution of this application.

Status of the Claims

Claims 1-3, 5-15, and 23-32 are currently pending and under examination. Claims 4, 16-22 have been canceled without prejudice or disclaimer of the subject matter claimed therein.

Amendments to the Claims

Claim 1 has been amended to recite the features of claim 4. Representative support can be found in claim 4 as originally filed.

Claims 5-7 and 26-28 have been amended to reflect the amendment to claim 1.

Claim 14 has been amended to place the claim in a better format for examination.

The amendments to the claims do not add prohibited new matter.

Rejection under 35 U.S.C. § 102(e)

Claims 1-11, 14, 15, and 23-30 have been rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Haas (U.S. Patent Application 20060128736).

The Office Action alleges that Haas discloses the claimed invention and that Haas teaches a method for making CPT-carboxylate formulations with empty nanoparticles. It is respectfully submitted that Haas does not disclose steps b) and c). As an example, Haas does not disclose providing empty nanoparticles and incubating an active agent with the empty nanoparticles. Haas only discloses a method wherein a lipid film is first formed in absence of the drug and the lipid film is subsequently resuspended in a buffer comprising the drug. The lipid film is not an empty colloidal nanoparticle. As defined on page 15 of the present application, a "colloidal nanoparticle" has a size range, with respect to all dimensions, of nanometers to micrometers and are not macroscopic. The lipid film, disclosed by Haas, extends to an area of millimetres or centimetres and thus is not a nanoparticle. Also, upon resuspension of the lipid film, the drug is encapsulated in the same instance that the nanoparticles (liposomes) are formed. Accordingly, this method disclosed by Haas does not disclose incubating an agent with an empty nanoparticle. Further, this method disclosed by Haas at paragraphs [0141] to [0144] involves

passive entrapment of the drug as the liposome is formed and is not a self-assembly process.

In summary, Haas only teaches a nanoparticle already containing a drug and passive entrapment of a compound by hydrating a lipid film with an aqueous solution containing the compound. Explicitly, Haas teaches that a lipid film comprising DOTAP and camptothecin may be prepared and then subsequently resuspended. The nanoparticles which comprise the drug are formed instantaneously upon resuspension in the aqueous phase. Consequently, Haas does not disclose empty nanoparticles because the nanoparticles formed upon resuspension already comprise the drug.

The Office Action alleges. It is therefore respectfully requested that this rejection be withdrawn.

Rejection under 35 U.S.C. § 103(a)

Claims 1-15 and 23-32 have been rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Burke (US Patent 5,552,156) in view of Perez-Soler (US Patent 5,834,012) and Allen (US Patent 6,316,024).

The Office Action acknowledges that Burke does not disclose cationic lipids and a mixing time of between 10 minutes to 6 hours and an incubation temperature between 4 °C and 25 °C. Burke only discloses the use of liposomes comprising DMPC, DSPC or DMPG for the encapsulation of campthotecin drugs. Table IV of Burke shows that DMPC and DSPC are neutral lipids and that DMPG is an anionic lipid. Thus Burke does not disclose the use of cationic nanoparticles. Further, Burke discloses that only the negatively charged lipid DMPG was able to bind strongly with topotecan. The Office Action alleges that dimyristoyl phosphatidylcholine (DMPC) has a cationic ammonium head group. This molecule, however, also comprises an anionic phosphatidyl which renders the molecule overall neutral. Accordingly, Burke does not disclose empty cationic nanoparticles.

The Office Action relies on Perez-Soler for disclosing cationic lipids. Perez-Soler discloses the use of cationic lipids to stabilize camptothecin in nanoparticles. However, Perez-Soler does not disclose a method of preparing nanoparticles comprising incubating the carboxylate form of camptothecin with empty nanoparticles. Perez-Soler only teaches passive entrapment of camptothecin in a cationic liposome to stabilize camptothecin. Accordingly, Perez-Soler does not disclose that camptothecin can self assemble with an empty cationic

nanoparticle.

The Office Action relies on Allen for disclosing forming liposomes with cationic lipids and incubating the liposomes with an active agent. Allen discloses the use of cationic lipids for forming liposomal compositions which may comprise camptothecin drugs. Allen discloses the preparation of liposomes comprising an active agent by: (i) passive entrapment of a water soluble compound by hydrating a lipid film with an aqueous solution of the agent; (ii) passive entrapment of a lipophilic compound by hydrating a lipid film containing the agent; and, (iii) active loading of an agent using a transmembrane pH gradient as the driving force (see col. 10, l. 3 ff). In methods (i) and (ii), passive entrapment of the drug occurs at the instant the liposome is formed. Like the Haas reference, as discussed above, these are not methods of self assembly. Method (iii) of Allen requires a step of establishing a transmembrane pH gradient which serves as a driving force for the encapsulation process. This process is described on page 3 of the present application and is distinguished from the steps required for the present invention. Particularly, the step of establishing the pH gradient disqualifies this method from being a "self-assembly process." Accordingly, the method described by Allen does not disclose the elements of the claimed invention.

Applicants therefore believe that the claimed method is not obvious under the references of Allen, Burke, and Perez-Soler. No reference discloses or suggests that camptothecin in a carboxylate form will self-assemble with an empty cationic liposome. No reference discloses a series of steps that would lead one skilled in the art to believe that cationic liposomes with camptothecin carboxylate can be prepared by loading empty cationic nanoparticles in a self-assembly process. The passive methods described by Allen all require that the active agent be incubated with the lipid prior to producing nanoparticles. Accordingly, these methods are distinct from the claimed invention.

Furthermore, there is no reason to combine the teachings of Perez-Soler or Allen, which are drawn to the use of cationic nanoparticles, with the teachings of Burke for obtaining colloidal nanoparticles comprising camptothecin carboxylate. No reference discloses that cationic liposomes are capable of self-assembly with the carboxylate form of camptothecin. Moreover, Burke states that camptothecin carboxylate has a low association with the liposomes as compared to other campothecin forms or derivatives and discloses that hydrolysis of camptothecin to its carboxylate form resulted in a three-fold reduction in binding to the

liposomes (see Burke at col 16, lines 6-8). Burke further discloses that the carboxylate form of camptothecin does not exhibit activity against a molecular target, is inefficient for treating cancer, and is toxic to healthy tissue (see Burke at col. 1, lines 50-55). Perez-Soler too discloses that the carboxylate form of camptothecin is less active (see Perez-Soler at col. 1, lines 42-45).

Accordingly, there is no reason to combine the teachings of the cited references because the cited references does not teach that camptothecin in a carboxylate form will bind to and self-assemble with a cationic liposome. Moreover, the cited references teach that the carboxylate form of camptothecin is undesirable as an active agent. It is therefore respectfully requested that this rejection be withdrawn.

Conclusion

The foregoing amendments and remarks are being made to place the application in condition for allowance. Applicants respectfully request entry of the amendments, reconsideration, and the timely allowance of the pending claims. A favorable action is awaited. Should an interview be helpful to further prosecution of this application, the Examiner is invited to telephone the undersigned.

If there are any additional fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-0310. If a fee is required for an extension of time under 37 C.F.R. §1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,
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